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An Overview of Allowable Total Error in the Clinical Laboratory.
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Guest: Dr. Kornelia Galior from Grady Memorial Hospital and Emory Medical School in Atlanta, Georgia.

Randye Kaye: Hello, and welcome to this edition of *JALM* Talk from *The Journal of Applied Laboratory Medicine*, a publication of the Association for Diagnostics & Laboratory Medicine. I'm your host, Randye Kaye. The allowable total error for an assay is a quality concept that defines the maximum amount of analytical error it can have to be effectively used clinically.

It includes the error contributions from both random and systematic error, which account for imprecision and bias, respectively. The performing laboratory needs to determine their own allowable total error limits for their assays, and there is no one-size-fits-all approach. The March 2026 issue of *JALM* features a review article that provides an overview of allowable total error and different methods of deriving it for clinical assays.

Today we're joined by the article's corresponding author, Dr. Kornelia Galior. Dr. Galior is a Director of Clinical Chemistry and Point-of-Care Testing at Grady Memorial Hospital and an Associate Professor in the Department of Pathology and Laboratory Medicine at Emory Medical School in Atlanta, Georgia. Dr. Galior's interests in the field of laboratory medicine focus on preventing laboratory errors, applications of biological variations, and defining quality metrics.

She is currently a member of the European Federation of Laboratory Medicine Task Group, involved with maintaining and improving the biological variation database, which will be quite relevant to our podcast today. Welcome, Dr. Galior. First off, what made you particularly interested in the concept of allowable total error?

Kornelia Galior: So it actually happened by chance. Right after my fellowship in my first job as a clinical chemist, the chemistry manager came to me and gave me my first project, which was to re-evaluate the allowable total error, also known as performance goals or quality goals, on all the chemistry tests we had at that time. And I remember how lost I was at first, because we had over 100 tests at that time.

And because it was my first job, I was trying to do my best. I remember that my first question was, "how did we get the

acceptance criteria that we are currently using in our laboratory?" And his response was that the previous leadership decided on these error limits.

So, I ended up learning about this concept much more than I anticipated. And then later on, my mentor, also a clinical chemist at the time, advised me to submit an ADLM roundtable proposal on this topic and that's how it all started.

Randye Kaye: Oh, wonderful. And you know, we should all do that in our first job, like go the extra mile and do what excites us.

Kornelia Galior: Exactly.

Randye Kaye: Yeah. So it's really clear you're excited about the topic. So, my next question is, why is knowing how to derive acceptance limits important in laboratory medicine?

Kornelia Galior: So, in my opinion, this topic is very important in the clinical laboratory, because laboratory personnel use these limits routinely. For example, before we implement a new instrument or a new test in the laboratory, we are required to perform method evaluation studies. And we will judge the acceptability of these studies using predefined allowable total error limits.

Another example when we use these limits is when we evaluate patient comparison studies during reagent lot-to-lot comparison or during six-month method correlations. We also use these limits when we have to do results corrections on patients after unacceptable QC event. And I realized how important it is to derive a limit that is not too wide, not too tight, and applicable to the testing method.

Randye Kaye: Okay. Yeah, I see why that's important. So now, what are some important considerations to think about when choosing allowable total error limits for an analyte?

Kornelia Galior: I think each analyte should have its own allowable total error limit established, and not one limit across all the analytes. The other important consideration is the format. We used to see allowable total error defined in percentage, but for some analytes that we evaluate at the lower end of the reportable range, we should also have measurement units defined as well. For example, in therapeutic drug monitoring, I would use both the measurement unit and the percentage as my acceptable criteria.

Another important consideration is given that these limits are used in various scenarios in the laboratory, we can think about budgeting of allowable total error in deriving a fraction of it and making it allowable limit. For example, when we

evaluate imprecision of the assay during method evaluation, imprecision is one of the errors affecting the test result.

So, every time I evaluate any test in my lab, either in the core lab or in point-of-care settings, I would use a fraction of allowable total error to evaluate imprecision results. Another example of budgeting allowable total error is during six-month correlation studies. I have seen using 50% of allowable total error to judge the acceptability of the study. So that's why it is important to derive the total allowable limit appropriately.

Randye Kaye: All right, thank you. So now let's talk about resources. What resources are available to derive these limits and which one do you recommend the most?

Kornelia Galior: All right, so interestingly, how to derive such limits in the laboratory has been a topic of discussions and debate for many decades. There were two major international conferences held in Europe that grouped different resources in different models and there are a lot of publications out there on this topic.

So what are the resources? Everyone is probably familiar that in the US, the limits in the laboratory may be based on the legal requirements. For example, CLIA set limits on a subset of analytes in routine chemistry, endocrinology, toxicology, or hematology.

These limits may be also set by providers of proficiency testing and external quality assessment schemes. For example, in US, CAP defines acceptable limits for each analytes in their survey. The resource that I am professionally the most involved is with allowable total error based on biological variation estimates, which is the inherent variation of an analyte around a homeostatic set point.

And one reason this model gained wide acceptance is that limits based on biological variation are based on the scientific data that has been published for various analytes since the 70s. Another advantage of using this resource is that there is an easily accessible and free database on biological variation that is constantly being updated and managed by the European Federation of Clinical Chemistry.

This working and task group conducts a meta-analysis of papers on the components of biological variations using Biological Variation Data Critical Appraisal Checklist from which the allowable total error is derived. So basically, they're ensuring the quality of the papers before they calculate the total allowable error. What is also helpful about this resource is that not only you can obtain a total allowable error from biological variation, but it also provides acceptable

limits for bias and imprecision in a three-level model defined as minimal, desirable, and optimal.

Another helpful resource when deriving allowable total error is based on professional recommendation, as they are based on extensive discussions among experts with a variety of professional experiences. But unfortunately, they are only available for a subset of analytes. You will also find allowable total error reported in the literature and package insert, which is the information provider for each test by the vendor, but the data could be skewed to show the best possible performance of the assay and not what's achievable in practice. The last resource I do want to mention is based on the state of the art and this is more of a model. However, this definition varies between peer review articles.

The European Federation of Laboratory Medicine describes the state of the art as based on the highest level of analytical performance technically achievable, linking the definition of the best quality of the test available. Other guidelines, on the other hand, describe the state of the art as typical analytical performance similar to peers using the same test method and where you can find these limits is from the peer group reported in the international providers of proficiency testing and external quality assessment schemes.

Now depending on which resources you will go with for your analyte, you will notice that allowable total error limits across different resources will differ in the magnitude. Recently, the Clinical Laboratory Standards Institute just published a guideline, EP46, that evaluates different resources and provide advantages and disadvantages for each and also shed some important insight into this topic.

Randye Kaye: All right. Thank you. So last question is about challenges. What challenges have you encountered when selecting allowable total error in your own laboratory?

Kornelia Galior: I think the biggest challenge I have come across is to provide resources for tests that are completely new tests or tests that provide results in a semi-quantifiable format. For example, multiple of blasts for urinalysis. I often have discussion with my colleague who oversees hematology, coagulation, and urinalysis on how to set allowable total error for hair analytes.

And this is quite difficult because there are no resources we can look up. CLIA only defines limits on the subsets of analytes. CAP often provides acceptable criteria on urine and body fluid analytes as 3-standard deviation and biological variation database currently does not provide limits for markers in fluid other than serum or plasma.

I think for tests like that, understanding their performance of these assays in stable operating situation and deciding on allowable total error subjectively would be how I would address it.

Randye Kaye: All right. Thank you. Well, thank you so much for joining us today.

Kornelia Galior: Thank you for having me.

Randye Kaye: That was Dr. Kornelia Galior describing the *JALM* review article, "An Overview of Allowable Total Error in the Clinical Laboratory." Thanks for tuning in to this episode of *JALM* Talk. See you next time and don't forget to submit something for us to talk about.